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1 PACKAGING AND DELIVERY OF PHARMACEUTICALS AND DRUGS

2 The present application claims priority from U.S. Provisional Application Serial
3 No. 60/214,578, filed June 28, 2000.

4 FIELD OF THE INVENTION

5 The present invention relates generally to the field of metering, packaging and
6 delivery of pharmaceuticals and drugs. Particular utility for the present invention is
7 found in the area of facilitating metering and packaging of medications and drugs for
8 inhalation therapy and will be described in connection with such utilities, although
9 other utilities are contemplated, including liquid medication applications.

10 DISCUSSION OF THE PRIOR ART

11 Certain diseases of the respiratory tract are known to respond to treatment by the
12 direct application of therapeutic agents. As these agents are most readily available in
13 dry powdered form, their application is most conveniently accomplished by inhaling
14 the powdered material through the nose or mouth. This powdered form results in the
15 better utilization of the medication in that the drug is deposited exactly at the site
16 desired and where its action may be required; hence, very minute doses of the drug are
17 often equally as efficacious as larger doses administered by other means, with a
18 consequent marked reduction in the incidence of undesired side effects and medication
19 cost. Alternatively, the drug in this form may be used for treatment of diseases other
20 than those of the respiratory system. When the drug is deposited on the very large
21 surface areas of the lungs, it may be very rapidly absorbed into the blood stream; hence,

1 this method of application may take the place of administration by injection, tablet, or
2 other conventional means.

3 It is the opinion of the pharmaceutical industry that the bioavailability of the
4 drug is optimum when the drug particles delivered to the respiratory tract are between
5 1 to 5 microns in size. When the drug particles need to be in this size range the dry
6 powder delivery system needs to address a number of issues:

7 (1) Small size particles develop an electrostatic charge on themselves during
8 manufacturing and storage. This causes the particles to agglomerate or aggregate,
9 resulting in clusters of particles which have an effective size greater than 5 microns.
10 The probability of these large clusters making it to the deep lungs then decreases. This
11 in turn results in a lower percentage of the packaged drug being available to the patient
12 for absorption.

13 (2) The amount of active drug that needs to be delivered to the patient may be of
14 the order of 10s of micrograms. For example, albuterol, in the case of a drug used in
15 asthma, this is usually 25 to 50 micrograms. Current manufacturing equipment can
16 effectively deliver aliquots of drugs in milligram dose range with acceptable accuracy.
17 So the standard practice is to mix the active drug with a filler or bulking agent such as
18 lactose. This additive also makes the drug "easy to flow". This filler is also called a
19 carrier since the drug particles also stick to these particles through electrostatic or
20 chemical bonds. These carrier particles are very much larger than the drug particles in

1 a capsule containing the powdered medication and the outlet channel is formed as a
2 mouthpiece protruding from the body. A capsule piercing structure is provided, which
3 upon activation forms one or more holes in the capsule so that upon vibration of the
4 capsule by an electro-mechanical vibrator, the powdered drug may be released from the
5 capsule. The piercing means disclosed in Wilke et al includes three radially mounted,
6 spring-biased piercing needles mounted in a trochoidal chamber. Upon hand rotation
7 of the chamber, simultaneous inward radial motion of the needles pierces the capsule.
8 Further rotation of the chamber allows the needles to be retracted by their spring
9 mountings to their original positions to withdraw the needles from the capsule. The
10 electromechanical vibrator includes, at its innermost end, a vibrating plunger rod which
11 projects into the intersection of the inlet channel and the outlet channel. Connected to
12 the plunger rod is a mechanical solenoid buzzer for energizing the rod to vibrate. The
13 buzzer is powered by a high energy electric cell and is activated by an external button
14 switch. According to Wilke et al, upon inhalation through outlet channel 3 and
15 concurrent pressing of switch 10d to activate the electromechanical vibrating means 10,
16 air is sucked through inlet channels 4 and 12 and the air stream through the secondary
17 inlet channel 4 raises the capsule up against the vibrating plunger rod 10a. The capsule
18 is thus vibrated rapidly with powder being fluidized and dispensed from the pierced
19 holes therein. (This technique is commonly used in manufacturing for dispensing
20 powder through a hopper where the hopper is vibrated to fluidize the powder and
21 move it through the hopper outlet. The pierced holes in the capsule represent the

1 • The performance of the prior art inhalers depends on the flow rate generated
2 by the user. Lower flow rate does not result in the powder being totally
3 deaggregated and hence adversely affects the dose delivered to the patient.

4 • Inconsistency in the bioavailability of the drugs from dose-to-dose because of
5 lack of consistency in the deaggregation process.

6 • Large energy requirements for driving the electromechanical based inhalers
7 which increases the size of the devices making them unsuitable for portable
8 use.

9 • Loss of medication from opened or topped capsules.

10 • Deterioration of medication in open or topped capsules due to exposure to
11 oxygen or moisture.

12 In my prior U.S. Patent Nos. 6,026,809 and 6,142,146 (with Abrams), we provide
13 an inhaler that utilizes vibration to facilitate suspension of a medication or drug into a
14 gas that overcomes the aforesaid and other disadvantages and drawbacks of the above
15 prior art. More particularly, the inhaler of our aforesaid patent includes a piezoelectric
16 vibrator for vibrating the medication or drug. In a preferred embodiment of our
17 aforesaid '809 and '146 patents, the medication or drug is supplied from a coiled tape
18 having a plurality of spaced blisters or wells for carrying controlled aliquots of a dry
19 powder medication or drug.

Referring to Fig. 1 which corresponds to Fig. 9 of our aforesaid '809 U.S. Patent, the medication or drug is packaged in a disposable drug cartridge 210 which includes a coiled tape 218 carrying a plurality of spaced flat walled blisters or wells 220 for containing controlled aliquots medication. A release film 221 covers and seals blisters or wells 220. Tape 218 is formed as a coil, and threaded between a first guide platen 222 and pinch roller 224. Pinch roller 224 in turn is driven by a take-up spool 226 which in turn is driven by a thumbwheel 228 which is mounted on a common shaft with the take-up spool 226. In use, release film 221 is peeled from the tape 218, whereby to open blisters or wells 220, one at a time, as the film is advanced through the cartridge, and the release film 221 is collected on take-up spool 226.

11 Completing cartridge 210 is a piezoelectric element 232 for mechanically
12 engaging the bottom wall of the opened blisters or wells 220, one at a time, as they are
13 selectively advanced in position over and in contact with the piezoelectric element 232.
14 Tape 218 also preferably includes detent means or the like for indexing the tape so that
15 a selected opened blister or well 220 is automatically positioned over piezoelectric
16 element 232. Finally, an actuating circuit and power supply (not shown) is mounted
17 within cartridge 210.

18 Preferably, but not necessarily, the interior walls of the housing are coated with a
19 metallized coating 234 so as to obviate possible electrostatic charge buildup within the
20 housing.

1 liquid medication or drug, particle size and dose of the medication or drug delivered
2 can be optimized, and tailored to the frequency of the piezo. Typically, the bottom
3 blister element is placed on/in close proximity to the piezo prior to or
4 contemporaneously with piercing the top element. The top element is pierced, and
5 activation of the piezo drives the medication or drug from the blister pack through the
6 perforations in the top element.

7 BRIEF DESCRIPTION OF THE DRAWINGS

8 Other features and advantages of the present invention will be seen from the
9 following detailed description, taken in conjunction with the accompanying drawings,
10 wherein:

11 Figs. 1a and 1b are schematic representations of a dry powder packaging and
12 delivery system in accordance with the prior art;

13 Figs. 2 - 5 illustrate various blister packs made in accordance with the present
14 invention; and

15 Figs. 6A and 6B illustrate a plurality of blister packs and piezos in accordance
16 with another embodiment of the invention.

17 DETAILED DESCRIPTION OF THE PRESENT INVENTION

18 Referring to Fig. 2, a blister pack in accordance with the present invention
19 comprises a bottom element 10 in the form of an elongate plastic tape or other flexible
20 material, e.g. cloth, foil, paper, etc., having an overlying top element 12, carrying a
21 plurality of spaced top crowned areas 14 containing controlled aliquots or doses of a

1 dry powder medication or drug or a liquid medication or drug. As illustrated in Fig. 2,
 2 the top crowned areas 14 are shaped as inverted cones and are mounted to bottom
 3 element 10 in regular spaced intervals. Areas 14 are substantially completely filled with
 4 a controlled aliquot or dose of a powder or liquid medication or drug. Typically, the
 5 blister pack of the present invention is provided as coil or a circular cartridge or unit
 6 dose pack. In use, the blister pack is uncoiled and advanced to a puncture stage where
 7 one or a plurality of controlled size holes 16 are punched through the top wall of the top
 8 crowned area 14.

9 The top crown areas 14 and bottom element 10 form an enclosed volume. The
 10 shape, height and volume of the blister pack, together with the size and number of
 11 holes punched through the top crowned area 14, play an important role in the de-
 12 aggregation and aerosolization of the powder or liquid material in the blister pack.

13 The three main phenomenon, besides others, which help in the de-aggregation
 14 and aerosolization of the material in the blister, are the Helm-Holtz resonator, the
 15 standing waves set-up in the blister pack and the vibrator frequency of the piezo. The
 16 Helm-Holtz resonator is formed by the holes punches in the top crown and the volume
 17 of the blister pack. The Helm-Holtz resonator helps to de-aggregate and eject the
 18 material from the blister pack. The frequency of the resonator will have to be optimized
 19 for maximum material de-aggregation and ejection efficiency.

20 The standing waves in the blister pack are determined by the height and shape of
 21 the blister. The standing waves help to lift and aerosolize the material in the blister.

- 1 advantageously may be employed for packaging and delivery of other wet or dry
- 2 materials including, for example, vitamins, hormones, steroids and other bioactive
- 3 small molecules, peptides, proteins, etc.
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